

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 9-11 are pending in the application, with 9 being the independent claim. Claims 1-8 and 12-22 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

35 U.S.C. § 112, second paragraph

In the office action dated March 30, 2005, the Examiner has rejected claims 9-11 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctively claim the subject matter which the applicant regards as the invention. The Examiner alleged that it is not definite by what is encompassed by the phrase "lipid-containing moiety" in claim 9. Applicants respectfully traverse this objection as it applies to the amended claims.

In the interest of advancing the prosecution of this application, Applicants have amended claim 9 to more precisely claim their invention. Applicants have amended claim 9 to define the term "lipid" to be a hydrophobic substituent, consisting of 4 to 26 carbon atoms, which when taken together with the attached carbonyl is a fatty acid acyl group. See Applicants' specification, page 5, lines 20-26; page 6, lines 19-21 and 23-27; and page 7, lines 19-21. Applicants respectfully submit that this objection has been overcome, and should be withdrawn.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 9-11 under 35 U.S.C. § 102(a), as allegedly being anticipated by Ekrami, H. dissertation ("the Dissertation"). Applicants respectfully traverse this rejection.

Applicants respectfully assert that the use of the Dissertation as a reference under 35 U.S.C. § 102(a) is not proper as the Dissertation is the Applicants' own work. Although the Dissertation lists Hossein M. Ekrami as the author, a rejection under 35 U.S.C. may be overcome by establishing that the portions of the reference pertinent to the claimed invention describe Applicants' own work. See *In re Katz*, 215 USPQ 14 (CCPA 1982). In the declaration under 37 C.F.R. § 1.132 ("Declaration"), attached as Exhibit A, Applicants state that the Dissertation discloses subject matter derived from Applicants' collaborative work notwithstanding the authorship of the Dissertation. Dissertations often list the graduating student as the author even if it contains collaborative work between the student and one or more academic advisors or collaborators. As stated in the Declaration, Wei-Chiang Shen was the academic advisor of the dissertation by Hossein M. Ekrami and this explains why the reference lists only one of the two Applicants as the author.

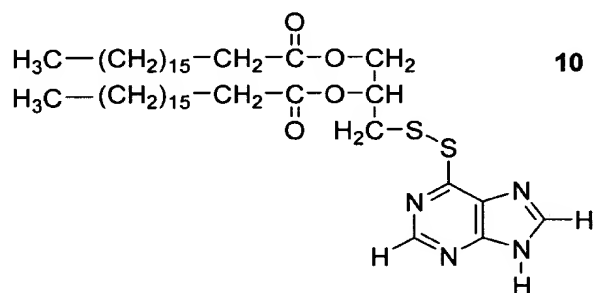
Thus, in light of the Declaration, the Dissertation cannot serve as a prior art reference in a rejection of the pending claims under 35 U.S.C. § 102(a). Accordingly, withdrawal of the rejection under 35 U.S.C. § 102(a) is respectfully requested.

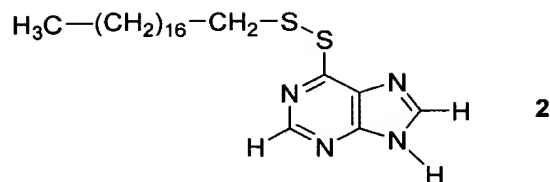
Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 9-11 under 35 U.S.C. § 103(a) as being unpatentable over Muller, C. E. *et al.*, *International J. Pharmaceutics* 57:41-47 (1989) ("Muller") in view of Chekhonin, V. P. *et al.*, *FEBS Letters* 287:149-152 (1991) ("Chekhonin") and Fix, J. A. *et al.*, *Am. J. Physiol.* 251:G332-G340 (1986) ("Fix"). Applicants respectfully traverse this rejection.

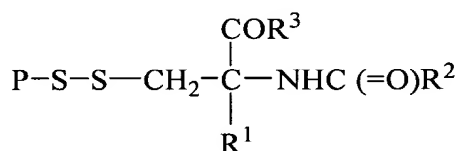
The Examiner stated that "[o]ne would have been motivated *to conjugate a protein, such as the peptide fragment disclosed by Chekhonin, V. et al. with a lipophilic compound using a disulfide bond* as disclosed by Muller, C. et al. to increase the concentration of a protein pharmaceutical in a site specific manner as suggested by both Fix, J. et al. and Chekhonin, V. et al." (Page 6, emphasis added.) This conclusion is not supported by the cited references.

In the office action, the examiner cites Muller for the synthesis of lipophilic prodrugs such as 6-MP by coupling a 6-mercaptopurine thiol derivative to lipophilic compounds via a disulfide bond and particularly points out compounds 2 and 10, which are reproduced below.





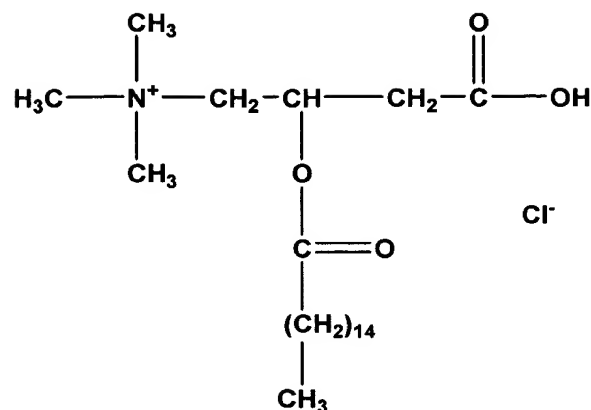
The drugs of Muller are totally unrelated to the compounds of the invention which have the following structure:



wherein R^1 , R^2 , R^3 and P are as defined in claim 9. There is absolutely no suggestion in Muller to modify compounds 2 and 10 to achieve the compounds recited in the claims. Therefore, Muller is a seriously deficient reference on which to base a *prima facie* case of obviousness.

The deficiencies of Muller are not cured by Chekhonin or Fix. According to the Examiner, Chekhonin discloses the coupling of fatty acid with fab-fragment peptides via an ester linkage. However, there is no suggestion or motivation in Chekhonin to couple a fab-fragment with a fatty acid via a disulfide bond. Moreover, there is no suggestion in Chekhonin to use the amino acid linker specified in claim 9.

Fix discloses fatty acids coupled with carnitine such as palmitoyl-DL-carnitine chloride having the formula:



There is no suggestion or motivation in Fix to couple a peptide, protein or oligonucleotide with a fatty acid via a disulfide bond and an amino acid linker. Thus, Checkhonin and Fix do not cure the deficiencies of Muller.

See *In re Grabiak*, 226 U.S.P.Q. 870 (Fed. Cir. 1985), wherein the court held that the Examiner had not presented a *prima facie* case of obviousness because the prior art did not suggest that one of ordinary skill in the art could substitute an oxygen atom for the sulfur atom in the claimed compound. According to *In re Grabiak*, replacing an ester with a thioester was not *prima facie* obvious absent a reference that shows or suggests to one of ordinary skills in the art that such an exchange may be made. Accordingly, the Examiner has not established a *prima facie* case of obviousness. Applicants therefore respectfully request that the rejection of claims 9-11 under 35 U.S.C. § 103(a) be withdrawn.

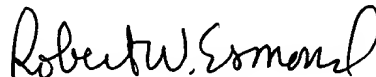
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond
Attorney for Applicants
Registration No. 32,893

Date: June 30, 2005

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
404451_1.DOC